Stratton VA Medical Center
IRB Standard Operating Procedure: Initial Review of Research

POLICY

It is Stratton VA Medical Center's policy to comply with all applicable federal, state, and local regulations, in the conduct of human subject research studies. (The reference to ICH Guidelines has been removed from this SOP) Written procedures are required for documenting expedited and full committee review of new protocols, and for reporting the IRB's actions to the Principal Investigator.

REFERENCE DOCUMENTS

45 CFR 46

21 CFR 50, 56

38 CFR 16

VHA Handbook 1200.5 Requirements for the Protection of Human Subjects in Research

PROCEDURE

Principal Investigators will request review of research by submitting a new complete initial submission packet.

Intake Review

The IRB Staff certifies that the Principal Investigator(s), co-investigator/s, sub-investigator/s, and research staff members listed on the form have completed the educational requirements and are credentialed to submit new research.

If the educational requirements are not met and credentialing is not verified, the IRB staff will inform the PI. The IRB will not review the research until the educational requirements have been met.

The IRB staff checks the original submission for completeness and accuracy and then enters the submission into the database.

If any items are missing, the IRB staff will notify the Principal Investigator(s) or the designated contact person in writing.

Scientific Review

All protocols will be required to have a form of scientific review. The ACOS/R in collaboration with the IRB Chair will determine which form of review will be used. Generally, scientific review of protocols will fall into one of two categories.

The first category is grant or other funded protocols: these protocols are typically given scientific review by the granting or funding agency. This level of review will be considered an adequate level of review for the IRB.

The second group is that of unfunded studies: these studies typically do not have a required external scientific review. Therefore, these studies will be assigned to two scientific reviewers. These reviewers' findings will be submitted to the IRB to used as part of the IRB human protection reviewing and approving role.

The ACOS/R and/or IRB Chairperson may at any time ask that any protocol be assigned two scientific reviewers despite its funding status.

In all cases of assignment of scientific reviewers, it will be the role of the ACOS/R and/or the IRB Chair to make the assessment and determination that the reviewer/s have the appropriate level of credentials and subject matter experience for review of each individual protocol. It will be expected that the reviewers do not have a conflict of interest or are directly involved in the specific protocol being reviewed. External reviewers will be appointed by the ACOS/R from outside sources when the protocols call for such review.

The expectation for scientific review will not be at the level of full peer or merit review, such as those applied to NIH funded studies. Rather, these scientific reviews will have the purpose of assuring basic scientific validity such that the research maximizes human subject benefits and minimizes subject risks.

During the Scientific Review, Reviewers will determine:

- The soundness of research design.
- The ability of the research to answer the proposed questions.
- The scientific review process provides the IRB the information it needs to determine whether the regulatory criteria for approval of research are met.
- The available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial.
- Clinical trials are scientifically sound and describe in a clear, detailed protocol.

Expedited Review

Research that represents no more than minimal risk and falls into one or more categories listed in "Categories of Research That May be Reviewed by the Institutional Review Board (IRB) Through an Expedited Review Procedure" may be reviewed by expedited review or by the full IRB. All other research must be reviewed by the full IRB.

The HRPP Coordinator consults with the IRB Chair or designee to discuss whether the research will be processed by full committee review or by expedited review.

Expedited Review Process

If it is determined that the protocol may qualify for expedited review, the entire submission packet is assigned to the IRB Chair who then may perform the expedited review or assign the protocol to an appropriate IRB designee. In either case, the reviewer must not have a conflict of interest. If a COI is declared by the assigned

reviewer, the protocol must be assigned to an appropriately designated IRB reviewer without a conflict of interest. An additional reviewer is assigned by the IRB chair (in consultation with the ACOS/R&D) primarily to review the scientific content if not already reviewed externally. The assigned reviewer conducts the review of the entire research submission, including the protocol, abstract, consent document(s), advertisements, participant materials, Conflict of Interest forms, HIPAA authorization and/or waiver request, PI and co-PI CV's, or other documentation evidencing qualifications, and applicable research grant or budget copy." The expedited review is performed with similar rigor as a full-committee primary reviewer.

The IRB chair will only designate trained IRB members to conduct review using the expedited procedure. These assignments will be made according to the education, experience, expertise and diversity of IRB members and their work-load.

The IRB Chair or designee conducting expedited review has the final authority in deciding whether the research qualifies for expedited review (all exempt research is reviewed as non-exempt/expedited research) and may recommend full committee review. The IRB will consider whether the proposed exempt and non-exempt projects support the VA mission and if there are any ethical or other issues.

If the reviewer requests changes or additional information, the reviewer may request that the IRB staff contact the Principal Investigator(s)or the designated contact person and requests the information.

Once the reviewer finds the research acceptable:

- The IRB Chair or designee who reviewed the research approves the research.
- The IRB Chair or designee completes the primary reviewer form and makes a declaration regarding conflict of interest. The primary reviewer should provide sufficient comments and summary of the project on the review form to indicate and justify the expedited category of review and indicate the rigor of review.
- The IRB Chair or designee signs and dates the IRB Initial Review approval letter and the 10-1223 Human Studies Subcommittee form, indicating the risk level and the interval of approval and protocol specific findings justifying any determinations required by the regulations.
- The IRB Initial Review approval letter, and copies of the approved stamped consent and HIPAA authorization, if applicable, is sent to the Principal Investigator(s).
- The IRB is notified of the approval in the agenda of the next scheduled IRB meeting.
- A copy of the Initial Review approval letter is filed in the Research Office with the approved stamped consent(s) and HIPAA authorization, if applicable.

- New research approved by Expedited Review receives an interval of approval of no more than one year.

Reviewers cannot disapprove research when using the expedited process.

Full Committee Review

Research that requires full committee review is placed on the agenda of the monthly IRB meeting and is distributed approximately one to two weeks in advance of the meeting. The agenda identifies all IRB members who are also participating in the research to alert the committee of a conflict of interest.

The IRB staff, with the concurrence of the IRB Chair or designee, assigns two primary reviewers with scientific or scholarly expertise, who are not participating in the research.

The IRB Chair may, at his/her discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond, or in addition to, that available on the IRB. The IRB will defer review to another IRB meeting or obtain consultation when there is not at least one person on the IRB with the appropriate scientific expertise to conduct an in-depth review. If an ad hoc reviewer is needed, the IRB Chair or Vice-Chair will make the appropriate contact, determine who will be contacted to serve as an ad hoc reviewer on the study or allow the convened IRB to determine who will be contacted to serve as a consultant.

Ad hoc reviewers are not considered IRB members and do not vote.

Any IRB member may request a ad hoc reviewer by making a verbal or written request to the IRB Chair or designee.

The IRB Chair or designee will review the qualifications of the ad hoc reviewer prior to the consultant's participation in the review of the research.

The consultant uses the primary reviewer form and would receive the full submission packet and documentation of key information provided by the ad hoc reviewer will be included in the meeting minutes.

If an ad hoc reviewer discloses a conflict of interest, it will be handled in the same manner as any IRB member (see IRB SOP Conflict of Interest).

Primary reviewers are expected to review a copy of the entire research submission, including the protocol, abstract, consent document(s), investigator brochure(s), advertisements, participant materials, Conflict of Interest disclosure forms, HIPAA authorization and/or waiver request, PI and co-PI CV's, and applicable research grants or budget copies approximately two weeks in advance of the meeting.

Primary reviewers are expected to review the DHHS-approved sample consent document and complete DHHS-approved protocols (when they exist).

Primary reviewers are provided with a Primary Reviewer Form to record their comments. It is expected that at least one reviewer performs an in-depth review of all pertinent documentation especially:

- Access to a population that would allow recruitment of the necessary number of participants.
- Sufficient time to conduct and complete the research
- Conflict of Interest
- Data security

Committee members who are not primary reviewers are given a copy of the full protocol submission packet, including the Informed Consent Form if applicable.

IRB members may ask the HRPP coordinator for any information that is provided to any other reviewer.

The review of research takes place at the monthly meeting of the IRB.

In order to approve a new research protocol, the IRB shall determine that criteria for approval of research are satisfied (38 CFR 16.111).

The IRB staff takes minutes at the meeting pertaining to discussion of the research and any controverted issues and their resolution.

Minutes are prepared within two weeks after the meeting and include:

1. The presence of a quorum throughout the meeting including the presence of one member whose primary concern is in a non-scientific area.

2. Attendance at the meetings including those members or alternate members who are participating through teleconference, and documentation that those attending through teleconferencing received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions.

3. Alternate members attending the meeting and for whom they are substituting.

4. The votes for, against, abstaining, recused, and excused, as well as the recommended period of approval. IRB members with a conflicting interest must recuse themselves from voting.
5. Actions taken by the IRB

6. Separate deliberations for each action

7. The names of IRB members who left the meeting because of a COI, along with the fact that a conflicting interest is the reason for the absence

8. Modifications or any other changes to the research required by the IRB.

9. The basis for requiring changes in or disapproving research.

10. A written summary of any discussion of controverted issues and their resolution.

11. Documentation of required IRB findings such as:

    - Alteration or waiver of requirements for informed consent
    - Waiver of requirement to obtain signed consent
    - Research involving vulnerable subjects

If the research is approved as submitted:

1 The IRB Chair or designee signs and dates the IRB Initial Review approval letter.

2 The Date of Approval is the date of the meeting at which the research was approved.

3 The IRB Initial Review approval letter, and copies of the approved stamped consent and HIPAA authorization, if applicable, is sent to the Principal Investigator(s).

If the research is granted approval with modifications:

- The modifications must be documented by the primary reviewer in sufficient detail to allow the IRB staff to verify the changes required by the IRB.
- A Notification of Approval with Contingencies letter, listing all required modifications and conditions for approval, is sent to the Principal Investigator(s).
- The Principal Investigator(s) responds to the Research Office with a copy of all modified documents within 3 months.
- The IRB staff reviews the modified documents for confirmation of all modifications required by the IRB.
- If the submitted documents have not been modified as required, the Principal Investigator(s) is contacted by IRB staff and asked to submit the complete revision as requested.
- Once the IRB staff determines that the documents contain all required modifications, the IRB Chair or designee signs the IRB Initial Review approval letter.
- The Date of Approval is the date of the meeting at which the research was initially approved, with modifications.

When the convened IRB requests substantive modifications or clarifications that are directly relevant to the regulatory criteria for approval of research, the response goes back to the convened IRB. Contingent modifications of the convened IRB not directly

relevant to the determinations required by the IRB are reviewed by the IRB chair or IRB member designated by the IRB chair.

If the Principal Investigator(s) does not return the required modified documents within approximately three months, as indicated on the Contingent Approval letter, the IRB Chair or designee notifies the Principal Investigator(s) in writing that the protocol remains unapproved and further consideration of this research will require submission of a new protocol.

If the research is disapproved:

- The IRB Chair or designee notifies the Principal Investigator(s) in a letter of the reasons for disapproval and offers the Principal Investigator(s) an opportunity to resubmit the research to the IRB within three months.

- If the Principal Investigator(s) resubmits the research to the IRB, the disapproval letter will be included in the primary reviewer materials for the next scheduled IRB meeting and distributed with the agenda.

- If a written response is not received by the deadline or the investigator does not contest the disapproval, the IRB Chair or designee notifies the Principal Investigator(s) in writing that the protocol remains unapproved and further consideration of this research will require submission of a new protocol.

The IRB may require proposed research to be reviewed and approved by the VAMC Radiation Safety Committee, Subcommittee on Research Safety & Biosafety (SRS&B), Institutional Animal Care and Use Subcommittee (IACUC), other committees of the VAMC, relevant committees of collaborating institutions, or by ad hoc reviewers with additional expertise not currently on the IRB.

Informed consent forms and HIPAA authorizations associated with approved research are stamped with a Date of Approval and a Date of Expiration. A copy of the stamped consent(s), HIPAA authorizations, and the original approval letter will be provided to the investigator.

The Date of Approval is defined as the date of the meeting at which the research was approved.

The Date of Expiration is defined as the Date of Approval plus the recommended interval of review; expiration date occurs at midnight on the last day that the protocol is approved.

A copy of the Initial Review approval letter is filed in the Research Office with the approved stamped consent(s) and HIPAA authorization, if applicable.

The research protocol and copies of documents received and sent are filed in the Research Office.

The IRB staff files the Primary Reviewer Form with the initial research submission

Standard Operating Procedures specific to Department of Defense Research

When the research is Department of Defense-sponsored research, all new research and substantive amendments to approved research must undergo scientific review prior to ethics (IRB) review.